SUBACUTE DEMYELINATING POLYNEUROPATHY. FIRST MANIFESTATION IN A CASE OF SPLENIC LYMPHOMA

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ABSTRACT

We present a 42 year-old man, admitted in Sibiu Neurology Clinic for pain, numbness, muscle weakness in the extremities, gait disturbance. The electromyography and nerve conduction studies examinations revealed a demyelinating polyneuropathy aspect in a biochemical context of pancytopenia and hypersplenism. Further hematology and histology evaluation statuated the diagnosis of splenic small B-cell lymphoma.

Key words: polyneuropathy, lymphoma

R.O., aged 42 years, male, living in rural area, former worker in a toxic environment, in present without occupation is presented in the Neurology Clinic with pain and paresthesia in the distal upper and lower limbs, decreased muscle strength, gait disturbance, with insidious onset approx. one month before admission. The condition worsens 3 days before admission. The medical history holds a respiratory infection three weeks ago without documentation. Clinically, pale skin, systolic murmur in the aortic area without neck irradiation, abdomen enlarged with a large spleen with the inferior pole near the midline. Neurologic examination: steppage gait, unable to walk on toes and heels, positive Romberg, absent achilean and styloradial reflexes, ectromelic hypoesthesia with extinction of proprioception and vibratory sensation in the legs. This outlines a diagnosis of anemic syndrome with splenomegaly and polyneuropathy syndrome.

Biochemical examination showed WBC – 3400/mmc, RBC – 3000 000/mmc, Hgb – 9.4 g%, Hct – 29.3%, MCV – 77 fL, MCH – 24.7 pg, RDW – 16%, PLT – 100 000/mmc, serum iron – 15 ug / dL, ESR – 30 mm / h, CRP – 57.8mg / L, VDRL – negative, protein electrophoresis – Alpha 1 globulin 4.5%. CSF examination: colorless, clear, 2 elements / mmc, Pandy + reaction, CSF proteins – 0.78 g / L, glucose – 72 mg%, chloride – 123.5 mEq / L. Nerve conduction studies revealed incalculable sensitive conduction velocity for median and ulnar nerves, motor conduction measured on median, ulnar, peroneal and tibial nerves showed decreased velocities with very low CMAP and significant dispersion of the signal; absent F waves. Needle EMG: wide MUP and poorer recruitment with minimal polyphase.

The electromiographic appearance advocated for a sensory and motor demyelinating neuropathy (fig. 1). Abdominal ultrasound showed a largely increased spleen (22/12.5 cm.) Osteomedular biopsy: bone marrow reacted on all lines, with interstitial infiltrates and focal nodular type and in a chronic lymphoproliferative process with small B-cell. The patient goes for surgery and splenectomy, liver biopsy, paracardial node removal are performed. Histopathology reveals a splenic small B-cell lymphoma, chronic B type viral hepatitis, periportal necrosis lymph node with small cell lymphocytic infiltration, confirmed by imunhistochemistry with CD20 positive. A positive diagnosis based on clini-

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Motor CV										
Test	Site	Stim point.	Lat., ms	Ampl., mV	Dur., ms	Area, mV x ms	Area increm., %	Dist., mm	Time, ms	Vel., m/s
2	right, Abductor digiti minimi, Ulnaris, C8 T1	wrist	10,3	**0,69**	10,2	3,8				
1	right, Abductor pollicis brevis Medianus, Ulnaris, C8 T1	wrist	17,1	**1,36**	12,5	8,5				
		elbow	25,1	**0,69**	10,4	2,9	-65,3	240	7,95	**30,2**
4	left, Abductor pollicis brevis, Medianus, C8 T1	wrist	26,3	**2,06**	13,5	2,7				
		elbow	33,8	**1,22**	12,9	7,4	-44,3	250	7,50	**33,3**
8	right, Abductor hallucis, Tibialis, I4 L5 S1	sole of the foot	28,1	**0,23**	31,8	2,7				
7	right, Extensor digitorum brevis, Peroneus, I4 L5 S1	sole og the foot	23,3	**0,09**	5,65	0,2				
		Fibular head	41,5	**0,39**	10,3	2,3	+1088	300	18,3	**16,4**

Figure 1. *Median, ulnar, peroneal and tibial nerves with very low speeds and very low CMAP and significant dispersion of the signal.*

cal and paraclinical examinations suggest a small B-cell splenic lymphoma, hypersplenism, subacute demyelinating polyneuropathy probably in infiltrative context, type B viral hepatitis.

The differential diagnosis is made by peripheral neurological disorders that occur in hematologic malignancies as acute lymphoblastic leukemia, Hodgkin lymphoma, non-Hodgkin's malignant lymphoma, multiple myeloma, Waldenstrom macroglobulinemia. The polyneuropathies occurring in malignant hematologic diseases are usually demyelinating and the majority of the authors use time criteria for distinguish them. Acute inflammatory demyelinating polyneuropathy (AIDP) by some authors identified with Guillain-Barre-Storhl, chronic inflammatory demyelinating polyneuropathy (CIDP) and multiple blocks motor neuropathy (MMN). AIDP is characterized by symmetrical loss of muscle strength, areflexia, sensory symptoms that usually precede motor deficit.

Progression takes about four weeks after that, in most of cases the condition improves. CSF appears dissociative between proteins and elements. It is also described in two subtypes: AMAN (acute motor axonal neuropathy) type and the demyelinating type. CIDP may appear as a progression or as a remission – recurrence type. Mumenthaler describes the subacute type as an intermediate form (SIDP) (1). MMN is considered a particular form of CIDP with motor conduction blocks, immune mediated, with a progressive deficit, fasciculation, cramps, usually without sensory symptoms. Considering the above criteria, we support a subacute demyelinating polyneuropathy (SIDP) in a malignancy context.

Under treatment with chemotherapy (cyclophosphamide, epirubicin and vincristine) and then associating the steroid and rituximab, the evolution is favorable with the disappearance of neurological symptoms and general amelioration.

The neurological and electromyography reassessment at 5 months shows a remarkable improvement in motor and sensory velocities (Fig. 2). At 9 months no significant improvement is observed (fig. 3).

The prognosis is reserved and taking into account the proliferation, invasion of bone marrow and other tissues, the surgical risk of splenectomy, and comorbidities (high viral replication of virus B to a year from diagnosis). In this case a particularity is considered to be the dramatic and otherwise sudden appearance of neurological symptoms before others.

DISCUSSIONS

Neurological manifestations in hematologic malignancies on the peripheral nervous system may be divided into specific: lymphomatous current compression, specific invasion of the nerves leading to demyelination; nonspecific by: sensorimotor neuropathy, demyelination of the posterior, lateral and anterior columns, total disappearance of the anterior horns neurons, the absence of nerve infiltration

Motor CV										
Test	Site	Stim point.	Lat., ms	Ampl., mV	Dur., ms	Area, mV x ms	Area increm., %	Dist., mm	Time, ms	Vel., m/s
2	right, Abductor digiti minimi, Ulnaris, C8 T1	wrist	4,95	**3,26**	7,65	14,9				
		elbow	12,9	**2,72**	9,20	13,6	-9,1	230	7,95	**28,9**
3	right, Abductor pollicis brevis, Medianus, C8 T1	wrist	6,85	**2,91**	7,05	9,5				
		elbow	11,6	**2,47**	9,00	8,3	-12,9	230	4,75	**48,4**
6	right, Abductor hallucis, Tibialis, I4 L5 S1	sole of the foot	10,3	**0,73**	6,90	3,2				
		popliteal fossa	22,3	**0,30**	4,10	0,7	-77,1	410	12,0	**34,2**
5	right, Extensor digitorum brevis, Peroneus, I4 L5 S1	sole of the foot	9,10	**0,64**	7,05	2,5				
Sensory CV										
4	n. Medianus	wrist	1,70	1,5	2,40	1,4		170	1,70	
1	right, n. Ulnaris	wrist	1,30	1,0	1,05	0,6		140	1,30	
7	right, n. Suralis, S1-S2	1	3,95	3,8	2,25	5,8		140	3,95	35,4

Figure 2. *5 months after the previous EMG – slightly increased motor velocities in ulnar, median and tibial nerves; increased CMAP amplitudes.*

Motor CV										
Test	Site	Stim point.	Lat., ms	Ampl., mV	Dur., ms	Area, mV x ms	Area increm., %	Dist., mm	Time, ms	Vel., m/s
2	right, Abductor digiti minimi, Ulnaris, C8 T1	wrist	5,20	**2,79**	12,9	18,9				
		elbow	13,6	**2,67**	13,4	17,4	-8,3	258	8,35	**34,1**
1	right, Abductor pollicis brevis, Medianus, C8 T1	wrist	7,35	**2,60**	15,7	10,7				
		elbow	12,1	**1,89**	15,4	10,1	-5,9	225	4,70	**47,9**
4	right, Extensor digitorum brevis, Peroneus, I4 L5 S1	sole of the foot	5,40	**0,83**	7,90	2,1				
		Fibular head	17,6	**0,80**	5,15	2,2	+2,9	355	12,2	**29,2**
Sensory CV										
3	right, n. Medianus III dig.	wrist	2,95	1,7	0,80	0,8		140	2,95	
5	right, n. Suralis, S1-S2	1	3,40	2,9	1,70	3,1		120	3,40	**35,3**

Figure 3. *At 9 months, without significant changes*

resembling a paraneoplastic syndrome. Hodgkin and non-Hodgkin lymphoma are leading quite often to abnormalities in nerve conduction velocities, destructive infiltration of the nerve, microembolisms in vasa nervorum.

Cases of Guillain-Barre syndrome (2) are most frequently described in Hodgkin's lymphoma, while in non-Hodgkin SIDP and CIDP predominates (2).

Up to 35% (3) of the patients with lymphoproliferative disease shows demyelinating neuropathy in the course of the disease as primary damage but also probably as a consequence of chemotherapy (bortezomib, vincristin, thalidomide, etoposide).

In terms of given data to clarify whether it is infiltrating nerve damage *per se* or just paraneoplastic manifestation, specialized studies (4) showed the need for biopsy and nerve specific

markers (anti-Hu, anti GM1, ANA, c-ANCA, anti-myelin associated glycoprotein) in combination with electromyography procedures in order to precisely diagnose the type of neuropathy. Suspicion for non-Hodgkin's lymphoma must be taken into account in patients who are diagnosed in a neurological service for inflammatory polyneuropathy of unknown cause (5).

REFERENCES

1. **Mumenthaler M. et al.** – Neurology, 4th edition, *Thieme*, 2004; 580-581
2. **Bradley W. et al.** – Neurology in clinical practice. Principles of diagnosis and management, 4th edition, *Elsevier* 2004; 826:1466
3. **Giglio P., Gilbert M.R.** – Neurologic complications of non-Hodgkin's lymphoma. *Curr Hematol Malig Rep* 2006 Dec; 1(4):214-219
4. **Blaes F., Tschernatsch M.** – Paraneoplastic neurological disorders. *Expert Rev Neurother* 2010 Oct; 10(10):1559-1568
5. **Gemignani F., Marchesi G., Di Giovanni G. et al.** – Low Grade Non-Hodgkin B-Cell Lymphoma Presenting as Sensory Neuropathy. *Eur Neurol* 1996; 36:138-141